

# XXVII

## Breast Cancer

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With the exception of skin cancer, cancer of the breast, at an incidence of over 65 per 100,000 population, far exceeds in frequency any other cancer in the female population. It has become the most common cause of death in women aged 40 to 44 and remains among the first three causes of death until age 60. The annual mortality caused by breast neoplasms is about 25/100,000 women.<sup>48</sup>

Primary treatment by modern surgery and radiotherapy results in a ten-year sur-

vival of 57% for operable cases. Earlier diagnosis can improve these results (Tables XXVII-1 and XXVII-2).<sup>20</sup> Seventy per cent of patients without axillary node involvement, but only 40% of operable cases with positive axillary nodes, survive 10 years. Size and histopathologic character of the neoplasm are correlated with curability. Tumor growth in about one-third of cases can be halted by endocrine manipulations and by chemotherapeutic agents.

Breast cancer was known and was treated

TABLE XXVII-1. Comparison of histologic types of infiltrating breast carcinoma

Histologic type	Infiltrating duct carcinomas with productive fibrosis (scirrhous carcinoma)	Infiltrating lobular carcinoma	Medullary (infiltrating)	Colloid (infiltrating)	Comedo-carcinomas (infiltrating)	Papillary (infiltrating)
% of total	78.1	8.7	4.3	2.6	4.6	1.2
Average age	50.7	53.8	49.0	49.7	48.6	51.9
Average size (cm.)	3.1	3.5	3.4	3.8	3.9	3.4
Node involvement (%)	60	60	44	32	32	17
Median survival of treatment failures	3.75	3.25	2.25	4.3	2.7	5
Actuarial survival						
5 years	59%	57%	69%	76%	84%	89%
10 years	47%	42%	68%	72%	77%	65%
20 years	38%	34%	62%	62%	74%	65%

From McDivitt, et al.<sup>21</sup>

1769

Exhibit F

oncogenic process would begin to produce morphologic changes in adolescence, and manifest a subtle and protracted course strongly influenced by early endocrine and reproductive experience, as MacMahon has proposed.<sup>32</sup> It would be accelerated by drug-induced mammary stimulation of protracted duration. Pregnancy would be a stimulus to growth for established tumors in many but not all cases. Exposure to radiation,<sup>45</sup> chemical carcinogens,<sup>34</sup> or immunosuppression<sup>66</sup> would accelerate the tumorigenic process, as has been shown for fluoroscopic exposure in tuberculous patients.<sup>39</sup>

### Pathology

Most breast cancers begin with neoplastic proliferation of the lining cells of small mammary ducts. The cells of the acini are apparently less frequently the source of neoplasia. Several independent foci of origin are often found in a mastectomy specimen,<sup>13</sup> and the disease is bilateral in 1 to 2% of cases at diagnosis.<sup>52</sup> The neoplastic cells proliferate in the lumen of the ducts and the acini, but also tend to break through the basement membrane and invade periductal tissues. From the connective tissue of the breast they incite a proliferation reaction.<sup>31</sup> Where fibrosis is minimal, the neoplasm often consists of an agglomeration of small spheroids or ovoids of regular and well-differentiated neoplastic epithelium, forming single layers about central luminal spaces. A thin supporting stroma is associated with these structures. Cells of these well-differentiated tumors have a regular structure, few mitoses, and minimal hyperchromatism. The rate of growth, extent of invasion, and frequency of lymph node metastases of 2- to 4-cm. tumors of this type are relatively low. About 25% of operable breast cancers are of this type.

From the level of structural and cytologic differentiation described above, a series of histologic forms manifesting less and less glandular organization leads finally to those cancers in which rapidly dividing, highly anaplastic cells are scattered in small groups

and rows through a field composed of proliferating reactive fibroblasts.<sup>31</sup> These undifferentiated cells spread into and along periductal lymphatics, veins, nerves, and tissue planes. Embolic metastases in regional nodes in the axilla and internal mammary chain may be abundant, whereas the primary lesion is still very small. These aggressive (grade III) cancers account for about 25% of cancers in most large series.

Infiltrating cancers, regardless of grade, all invade the breast parenchyma. Their permeation extends toward the areola, which overlies a lymphatic plexus formed by confluence of lymph channels paralleling the 20 mammary excretory ducts.<sup>55</sup> Extension also develops back along the deep lymphatics to the pectoral fascia and thoracic wall.<sup>16</sup> Characteristically, the fibrosis accompanying cancerous invasion induces contractures along the fascial structures and planes of the breast.<sup>16</sup> These fix the neoplasm to the skin and chest wall and retract the nipple. Lymphatic permeation causes restriction of lymph flow and skin edema. This often is associated with superficial vascular dilatation, which is responsible for the heat and redness over locally advanced lesions. Blood leaving the metabolically active neoplasm is hotter than that from normal breast tissue. The heat differential in tumor-draining veins reaching the subcutaneous region provides the basis for thermographic cancer detection.<sup>10</sup>

Infiltrating duct cell cancers, which invade the breast widely and invoke proliferative fibrosis, account for 80% of all mammary cancers.<sup>31</sup> A common name for these neoplasms is scirrhous carcinoma (Table XXVII-1).

Comedocarcinoma is a variety of duct cell mammary cancer which manifests its main growth potential by filling the larger mammary ducts with solid cords of cancer cells. It less commonly metastasizes to the lymph glands than does scirrhous carcinoma. About 5% of mammary cancers belong in this category. Papillary carcinomas are the least frequent of duct cell cancers and also have a relatively favorable prognosis.<sup>31</sup> (Table XXVII-1).

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reactive fibrosis or contractures and are less  
invasive than scirrhous carcinoma constitute  
about 7% of all cases. One of these, the  
medullary type, grows in a circumscribed  
rather than a stellate gross form, is com-  
posed of uniform sheets of cells, and is infil-  
trated by lymphocytes and plasma cells.  
Another is the mucoid carcinoma, in which  
large masses of mucus-producing cells also  
grow as a large, soft, globular, and well-  
delineated mass (Table XXVII-1).

The invasive lobular cancers, however, do  
not differ notably in age distribution or  
prognosis from infiltrating duct-cell cancers  
with productive fibrosis.<sup>31</sup>

Multicentric "lobular carcinoma in situ"  
is not an invasive malignant lesion. It is  
bilaterally demonstrable on biopsy in 30%  
of cases.<sup>31</sup> It is not certain that the invasive  
cancers that some women with this diagnosis  
are found to have at the time of prophylac-  
tic mastectomy or develop later in breasts  
previously subjected to biopsy stem from the  
lobular dysplastic foci themselves. Whether  
mastectomy is indicated for this diagnosis  
remains controversial, but at the least very  
close surveillance is required, since the  
20-year risk of invasive cancer development  
in patients with this disorder is at least 25%.  
This lesion is not recognizable clinically.

**Regional Lymph Node Pathology.** The  
number and locus of lymph node metastases  
in the axilla (Table XXVII-2), the involve-  
ment of internal mammary nodes, metasta-  
ses in the supraclavicular nodes, and extra-  
capsular invasion from nodal metastases  
into adjacent tissues have important prog-  
nostic implications.<sup>46</sup> Sinus histiocytosis in  
lymph nodes is disputed as regards progno-  
sis and may represent evidence of an im-  
munologic reaction against the neoplasm.<sup>28</sup>

The axillary nodes are commonly divided  
into three anatomic groups (Table  
XXVII-2). Group I is lateral and inferior  
to the pectoralis minor. Group II lies be-  
neath it and receives efferent tributaries  
from group I. The highest level, group III,  
lies medial to the pectoralis minor in the  
apex beneath the clavicle (Table XXVII-2).  
Where only the lower axillary nodes are  
involved, and less than four nodes contain  
metastases, five-year survival rates are about

60% as compared to 80% for node-negative  
cases.<sup>46</sup> However, when the number of posi-  
tive nodes is larger, and particularly when  
the higher apical group contains cancer,  
five-year survival is only about 30% (Table  
XXVII-2). Long-term survival probability  
is reduced from 40% ten-year survival in all  
node-positive cases without perinodal inva-  
sion to 12% in those with perinodal invasion.  
When supraclavicular nodes contain gross  
metastases, the five-year survival is less than  
10%.

In general, internal mammary nodes are  
not involved when less than 4 axillary nodes  
are positive, unless the tumor is large and  
medially located. But if numerous axillary  
metastases are found, more than one-third  
of cases have positive internal mammary  
nodes.<sup>20</sup>

Cancer extends from the breast and the  
axillary and internal mammary nodes to the  
supraclavicular nodes. About one-fifth of  
patients who die of mammary cancer de-  
velop disease in the homolateral supra-  
clavicular nodes during the course of their  
illness.<sup>20</sup>

**Distant Metastases.** The leading sites of  
distant metastases are the lymph nodes, the  
lungs, red bone marrow, liver, and bone  
(Table XXVII-3). The pattern of dissemi-  
nation is predominantly hematogenous.<sup>57</sup>

TABLE XXVII-3. Sites of metastases at au-  
topsy (432 cases)

Site	Number of cases	% of cases
Distant lymph nodes	277	64
Lung	247	57
Regional nodes	230	53
Liver	218	51
Bone	213	49
Adrenal	148	34
Skin	124	29
Ovary	53	12
Spleen	52	12
Pancreas	49	11
Kidney	46	11
Brain	42	10
Thyroid	35	8
Heart	22	5

Data from Meisner and Warren.<sup>32</sup>

The skin and distant lymph nodes are commonly involved by multiple lesions. Pleural lesions may occur in patients without radiographically visible pulmonary metastases, and malignant pleural effusion is often the first site of recurrence.

Dissemination occurs early and regional lymphatic metastases are not a necessary intervening step in the process. Nevertheless, at least 30% of cases with as many as seven positive axillary nodes, that is, cases in which the regional node filter (circa 35 nodes) remains in large part free of cancer, are disease-free 10 years after radical mastectomy,<sup>20</sup> which strongly indicates that a significant proportion of these cases can be cured by eradication of regional neoplastic foci, even after embolic dissemination of cells through lymphatic channels has begun.

There is a well-established positive correlation between the degree of regional node involvement and the extent and timing of distant metastases which favors the view that regional nodes provide a focus for hematogenous spread.<sup>21</sup>

### Diagnosis of Breast Cancer

The recognition of breast cancer is not difficult in most cases. A hard-circumscribed mass, which does not move freely in the breast and is clearly felt with the flat surface of the fingers, is the classic breast cancer. When fixation to skin, nipple retraction, skin edema, or deep fixation is present, it is nearly certain that the lesion is malignant.

However, all these features can be produced in some degree by benign or inflammatory lesions. Consequently the one rule of importance is that every solitary mass found in the breast and not proved to be a cyst must be subjected to biopsy.

The problem of diagnosis is not so much the recognition of the nature of a cancerous mass as the finding of small lesions not known to the patient. This should be a major aim of every physical examination in adult women. It requires thorough palpation and inspection of the breast.

Palpation is best performed with the

breast stretched over the hyperextended thoracic wall, a position attained by placing a rolled towel or small pillow under the prone patient's lower thorax. Palpation should be done with the arm resting at the side, and also with it abducted but supported passively on the side being examined. Palpation is done with the palmar surfaces of the fingers and should be gentle and systematic, beginning with the areolar area and covering the entire protuberant breast as well as the axilla.

Careful inspection for underlying prominences, asymmetries, nipple retraction or tilting, and dimpling or edema of the skin should be performed, not only during palpation, but also (1) with the patient sitting up facing the examiner, (2) during the slow raising of the arms from the sides to meet above the head, (3) with the patient leaning forward to allow the breast to depend maximally from the chest wall, and (4) with tension on the pectoralis muscles, achieved by having the patient press her hands against her hips. All these maneuvers are aimed to betray the contracture of breast ligaments and ducts by small, invasive, deep-lying, infiltrating lesions. In well-equipped institutions, mammography and thermography should be employed regularly in women over 35 and in younger women with breast complaints, cystic disease, or a family history of breast cancer, and those who have not borne a child prior to age 25, have sterility problems, or are taking contraceptive steroids.

Breast cancer must be found when it is very small, one centimeter or less in diameter, to achieve an optimal probability of cure.<sup>20,49</sup> The average lesion that women currently bring to the attention of the physician is 3 to 4 cm. in diameter.<sup>31</sup> In 45% of such cases, multiple positive axillary nodes are present and prognosis is poor.

In the great cancer centers throughout the world, surgeons take at least six premenopausal patients to biopsy for questionable breast masses for every breast cancer they find. Conversely, in postmenopausal patients, all but one of six lesions leading to biopsy are malignant.